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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,139	12/17/2002	Anne Eckert	ST99042USPCT	1457

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
03/11/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/088,139	ECKERT ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,8-12,17-20 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,8-12,17-20 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of June 18, 2009 on December 17, 2009.

Claims 1-5, 7, 13-16, 21 are cancelled.

Claims 6, 8-12, 17-20, 22-25, drawn to a method for detecting compounds that treat neurodegenerative disease comprising exposing compounds to a transgenic non-human animal expressing a multimutated form of presenilin 1, are under consideration.

Maintained Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 8-12, 17-20, 22-25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Citron et al., 1998, Neurobiology of Diseases, 5: 107-116 in view of St. George-Hyslop et al., US Patent 6,395,960, patented May 28, 2002, Ishii et al., 1997, Neuroscience Letters, 228: 17-20, Borchelt et al., 1997, Neuron, 19: 939-945, and Xia et al., 1997, The Journal of Biological Chemistry, 272: 7977-7982, for reasons of record, June 18, 2009.

Applicant's arguments filed December 17, 2009 have been fully considered but they are not persuasive.

Applicant indicates that on page 5 of the Action, the Office Action alleges that at the time of filing, the art teaches that peripheral cells that expres mutant PS1 exhibit apoptosis (St. George-Hyslop et al., col. 20, 3rd parag.). Applicant indicates that no statement can be found in the review of cols. 19 and 20. Applicant requests an affidavit under 37 CFR § 1.104(d)(2) (Applicant's response, pages 4-5). In response, the teaching of mutant PS1 protein being associated with apoptosis is taught in col. 20, 3rd parag. of St. George-Hyslop et al. The paragraph has been copied below for Applicant's convenience. The Examiner has underlined and bolded the text that teaches mutant PS1 protein being associated with apoptosis in peripheral tissue.

> The normal PS1 protein, substantially free of other proteins, is encoded by the aforementioned SEQ. ID No:1 and SEQ ID NO:133. As will be later discussed, PS1 protein and fragments thereof may be made by a variety of methods. Purified **mutant** PS1 protein is characterized by FAD--associated phenotype (necrotic death, **apoptotic** death, granulovascular degeneration, neurofibrillary degeneration, abnormalities or changes in the metabolism of APP, Ca.sup.2+, K.sup.+, and glucose, mitochondrial function and energy metabolism neurotransmitter metabolism, all of which have been found to be abnormal in human brain, and/or **peripheral tissue cells** in subjects with Alzheimer's Disease) in a variety of cells. The mutant PS1, free of other proteins, is encoded by the mutant DNA sequence.

Applicant indicates that the methods of claims 6, 8-12, 17-20, 22-25 cannot be properly be said to be prima facie obvious. The primary references are discussed above. The secondary references are not alleged to remedy the noted deficiencies of the primary references. First, there is no suggestion or motivation in the art that is cited in the Office Action to modify or combine the references teachings to detect compounds

intended for the treatment of neurodegenerative diseases. Second, there is no indication of reasonable expectation of success. The references are concerned with producing Abeta42 and provide no expectation that the cells designed for production would apoptose. Simply protein producing cells would not be expected to apoptose as cell must be viable for protein production. Secondary references are alleged to teach specific mutations. These teachings do not remedy the deficiencies of Citron. Finally, the prior art references (or when the references are combined) cannot properly be said to teach or suggest all claim limitations. Making a transgenic animal as a source of peripheral cells for transgenic monitoring is not suggested in the applied references. For example, Citron teaches production of "double transfected cell lines" for studying Abeta42 production (see page 108, 2nd col., top parag.). There is no suggestion to produce a transgenic mammal and then to use that mammal for "detecting compounds intended for the treatment of neurodegenerative diseases (Applicant's response, pages 5-6). In response, this is not persuasive. While the Examiner has not explicitly indicated that animal models of diseases (or cells of animal models of disease) are used in screens for medicaments, it is understood in the art that animal models of disease are used to study the etiology and pathology of disease and are also used to screen for medicaments. For explicit teaching that animal disease models (and their cells) are used to screen for medicaments, St. George-Hyslop et al. teach in their situation that presenilin proteins and nucleic acids may be used in the screening of small molecules which will be candidates for drug therapy of Alzheimer's and related diseases. In one embodiment, small molecules may be screened for their ability to bind to a presenilin.

Assays are provided which may be used to identify small molecules which bind selectively or preferentially to either normal or mutant forms of presenilin. Such small molecules may be further tested using animal models to further evaluate their therapeutic utility. Another assay includes determining whether a compound has the ability to induce or repress expression of presenilins. Assays are provided in which the ability of the compound to alter the levels of presenilin mRNA transcripts or protein in a cell or cell culture is tested (St. George-Hyslop et al., col. 5, 4th parag.). Given St. George-Hyslop et al.'s teaching, an artisan would recognize that one could take cells from a non-human mammal and use it to screen for compounds that can be used to inhibit mutant presenilin and in turn be used to treat symptoms associated with mutant presenilin.

With regard to Applicant indicating that there is no reasonable expectation of success that the cells designed for production would apoptose (Applicant's response, page 5), this is not persuasive because St. George-Hyslop et al. teaches that cells that overexpress mutant presenilin apoptose (see St. George-Hyslop et al., col. 20, 3rd parag.). With regard to Applicant indicating that simply producing cells would not be expected to apoptose as cells must be viable for protein production, it is noted that the cells are viable at the start and eventually apoptose as the cell accumulates mutant presenilin. An artisan would recognize that one could screen for medicaments that reduce or stop the accumulation of mutant presenilin and thus stop or reduce the incidence of apoptosis.

With regard to Applicant indicating that the cited art does not teach making a transgenic animal as a source of peripheral cells for monitoring (Applicant's response, page 5), St. George-Hyslop et al. teach that cells can be obtained from an animal model of disease and that these cells can be used to screen for compounds that could be used as medicaments (St. George-Hyslop et al., col. 5, 4th parag.).

Thus, the claims remain rejected.

It is noted that the rejection of claims 1-5, 7, 13-16, 21 are withdrawn as the claims are cancelled.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Primary Examiner
Art Unit 1632